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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,654	11/05/2001	Gotz Nowak	ALBRE17	5284

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EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,654	NOWAK ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,12,15,17 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,12,15,17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/12/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: figure 1 should be submitted by amendment.

DETAILED ACTION

Claims 9, 10, 12, 15, 17, 19 are pending and are considered on the merits.

Claim Rejections - 35 USC § 112

Claims 9, 10, 12, 15, 17 are/remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims now include a standard curve in the kit; however, no standard curve was included in the kits disclosed in the specification or original claims. Contrary to the inserted new matter requiring the inclusion of a standard curve, the instruction is given in the working example to replace the standard sample which is used to generate the standard curve with the unknown. That is, the instruction seems to be to generate a standard curve in each laboratory for each putative inhibitor and use it to determine the concentration of each inhibitor. The standard curve would reasonably be expected to be distinct for each distinct inhibitor as the degree of inhibition of coagulation per mass/volume of each inhibitor would be distinct. For example, a gram/l of hirudin would not be expected to have the same inhibitory value as a gram/l of EDTA or heparin. Further, no Fig. 1 (the standard curve) appears in the as-filed specification. There is only a mention of a non-existent Figure 1 in the example.

Response to Arguments

Applicants have argued that Figure 1 was present in the National Phase of the PCT. As this appears to be a correct statement, applicants may insert the figure with translated X axis label by amendment to the specification and it will be entered as being part of the original specification.

However, for the reasons above, the inclusion of a standard curve in the packaging of the kit reagents is still considered to be new matter. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept of the insertion of printed standard curve. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the concept. If it does not, the material is new matter. New references purporting to demonstrate what is routine in the art cannot demonstrate the possession of a concept after the fact.

Claim Rejections - 35 USC § 102

Claims 9, 10 and 12 remain rejected under 35 U.S.C. 102(b) as being anticipated by Han *et al.* [AU].

The claims are directed to a kit comprising:

1) a solution of a coagulation-inhibiting substance not interfering in the transformation of prothrombin into active meizothrombin or meizothrombin fragment 1,

2) a chromogenic or fluorogenic substance dissociable by active meizothrombin or meizothrombin fragment 1,

3) a solution of a substance dissociating prothrombin into meizothrombin or meizothrombin fragment 1

4) standard curve, which is printed matter.

Claim 12 further has a solution of prothrombin.

The references are relied upon as explained below.

Han *et al.* disclose components comprising 1) antithrombin, 2) tosyl-Gly-Pro-Arg-p-nitroanilide and 3) factors Xa, Va and phospholipid. They are used in a test of inhibition of prothrombin activation products by antithrombin (Fig. 4). Thus, these chemicals have been assembled in the prior art for a similar purpose, that is, the testing of the inhibition of the coagulation process by a thrombin inhibitor.

Insofar as the composition claims rely on the inclusion of components which instead of being characterized by technical features suitable for the identification of components which are compounds, is imprecisely defined by means of functional features which merely recite the desired result to be achieved, the subject matter is considered to be anticipated by the disclosure of the prior art.

Response to Arguments

Applicants argue that the kit composition contains a standard curve which is not disclosed as being part of the kit composition of the prior art.

Although the prior art does not include a printed standard curve, the printed matter does not interrelate with the assemblage of reagents to as to produce a new product in the sense of *In re Gulack*, 703 F.2d 1381 (Fed. Cir. 1983). Rather, since the kit does not depend on the printed matter and the printed matter does not depend on the kit, an anticipatory rejection over Han *et al.* is sustainable, see *In re Ngai*, 70 USPQ2d 1862 (CAFC 2004).

Claim Rejections - 35 USC § 103

Claims 9, 10, 12, 15, 17 and 19 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,547,850 [AA] in view of US 5,702,912 [A] or Houbouyan *et al.* [U].

The claims are directed to a kit comprising:

1) a solution of a coagulation-inhibiting substance not interfering in the transformation of prothrombin into active meizothrombin or meizothrombin fragment 1, such as heparin,

2) a chromogenic or fluorogenic substance dissociable by active meizothrombin or meizothrombin fragment 1, such as a p-nitroanilide type substrate,

3) a solution of a substance dissociating prothrombin into meizothrombin or meizothrombin fragment 1, such as ecarin,

or the direct substitution of 3) by meizothrombin or meizothrombin-des fragment 1

4) a standard curve which is printed matter.

and in claim 19,

5) hirudin.

Claim 12 is directed to the inclusion of a separate solution of prothrombin as another component in the test kit.

US 5,547,850 discloses a composition comprising:

1) heparin,
2)
3) ecarin,
4) meizothrombin and/or meizothrombin-des-fragment 1 (col. 2, l. 26-33).
5) hirudin (col. 5, l. 10).

The composition is used for the determination of hirudin and other thrombin inhibitors.

The composition lacks (2) the chromogenic substrate which produces p-nitroanilide for spectrographic analysis and the inclusion of a separate vial of prothrombin.

The detection of the end point of the reaction is performed with an electrically triggered coagulation test (col. 3, l. 39). This test is also known as the ecarin clotting time test.

US 5,702,912 discloses an assay for determining the concentration of inhibitors of thrombin where the assay for the activity of thrombin may be either a coagulation (clotting) test or a chromogenic substrate for thrombin such as S2238 (Kabi) which is read spectroscopically (col. 5, l. 61-67). The reagents are:

1) clotting factor reagent comprising prothrombin, antithrombin III,

2) chromogenic substrate for thrombin (S2238) and EDTA and

3) activator

5) hirudin, example 3.

Houbouyan *et al.* disclose the equivalency of the chromogenic method of detection (amidolytic method) which is read spectroscopically and the clotting end point for the determination of the concentration of thrombin inhibitors present in a sample. Both measure thrombin activity. The chromogenic substrate is S2238 which releases p-nitroanilide for spectroscopic analysis at 405nm.

The substitution of the chromogenic assay for the clotting assay in the method of '850 would have been obvious when taken with '912 or Houbouyan *et al.* who disclose the equivalency of such a substitution for the determination of thrombin activity. Therefore, the addition of a chromogenic substrate to the

composition of '850 in order to detect the activity of thrombin spectroscopically in a chromogenic assay instead of a clotting end point would have been obvious.

The addition of an individual solution of prothrombin to the kit would have been obvious as it may be used with hirudin or analogs of hirudin to generate standard curves in non-plasma samples which may not have sufficient native prothrombin concentrations for performance of the assay or it may be used for the generation of the meizothrombin or meizothrombin-des-fragment 1 with ecarin for use in the assay.

One of skill in the art may detect the activity of thrombin in any manner known in the art for the performance of an ecarin-mediated, thrombin inhibitor test as suggested by the references with a reasonable expectation of success.

Please refer to the reasoning in In re Ngai cited above for the qualification of printed matter in a composition to distinguish the known composition from the prior art.

Applicants' arguments filed 8/25/04 and 10/5/04 and 11/29/04 have been fully considered but they are not persuasive for the reasons above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. The examiner can normally be reached on Monday, Tuesday, Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (703) 308-4742. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sandra Saucier
Primary Examiner
Art Unit 1651